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Spontaneous movements associated with rocuronium: is pain on injection the cause?

A. BORGEAT AND D. KWIATKOWSKI

Summary

Spontaneous movements are sometimes observed of the arm into which rocuronium is administered. In order to assess a possible relationship between these movements and pain, we injected in 10 awake, ASA I patients, in a double-blind manner, both rocuronium 1 ml (10 mg) and 0.9% NaCl 1 ml (placebo), with a 30-s interval in between. None of the patients receiving placebo complained of pain, but eight of 10 patients reported a strong burning pain during injection of rocuronium with brisk flexion of the elbow and wrist, similar to those observed in patients after induction of anaesthesia. A second injection of rocuronium did not produce such pain and no movements were observed. We conclude that injection of rocuronium is associated with severe, burning pain of short duration, responsible for the spontaneous movements in the arm observed after induction of anaesthesia. (*Br. J. Anaesth*. 1997; **79**: 382–383).

Key words
Neuromuscular block, rocuronium. Pain, injection.

Rocuronium bromide is a new steroidal non-depolarizing neuromuscular blocking drug, related structurally to vecuronium and characterized by a rapid onset and intermediate duration of action.[1 2]

In the recent past, we observed in some patients the occurrence of sudden flexion, lasting 10–20 s, of the wrist and arm into which rocuronium was infused. Although this compound is considered to be tolerated well during injection, recent reports indicate severe burning pain after i.v. injection of rocuronium.[3–5]

The aim of this study was to assess and characterize the nature of the pain and to investigate the possible association between pain and spontaneous movements during administration of rocuronium.

Methods and results

After obtaining institutional Ethics Committee approval and informed patient consent, we studied 10 patients, ASA I, aged 20–40 yr, weighing more than 70 kg and undergoing elective orthopaedic surgery.

All patients were premedicated with midazolam 0.1 mg kg^{-1} orally, 1 h before induction of anaesthesia. An 18-gauge i.v. cannula was inserted into the dorsum of the hand and a tourniquet inflated slowly on the same side until the patient considered it uncomfortable; then it was deflated by 10 mm Hg in order to create venous stasis without any pain. In the first part of the study each patient received randomly, in a double-blind manner, both rocuronium 1 ml (10 mg) and 0.9% NaCl 1 ml (placebo) with an interval of 30-s in between. The vials were stored at room temperature at least 2 h before administration and were prepared and coded by an independent investigator. Thirty seconds after administration of the second drug, the tourniquet was deflated slowly and the patient received a bolus dose of propofol 3 mg kg^{-1} in order to assure rapid induction.

In the second part of the study another five patients received two successive injections of rocuronium 1 ml (10 mg) at 30-s interval, following the same procedure as described previously.

In the third part of the study 10 more patients received two successive injections of either 0.9% NaCl 1 ml (pH 5.3) or 0.9% NaCl 1 ml adjusted to a pH of 4, according to the same procedure as described previously. NaCl 0.9% was buffered at pH 4 by adding 20% hydrochloric acid 0.02 ml to 0.9% NaCl 1000 ml (ABL 505 Radiometer Copenhagen). The vials were prepared and coded by our pharmacist.

Pain was scored on a VAS from 0 = no pain to 10 = strongest pain imaginable. The patient, when pain was present, was asked to orally score its intensity and describe its nature. Any movement associated with pain was observed carefully by one of the investigators.

In the first part of the study no patient felt any pain (VAS = 0) when receiving placebo. Eight of 10 patients complained of severe pain during injection of rocuronium (VAS = 10) which lasted for approximately 10–20 s; one patient reported moderate pain (VAS = 5) and the last patient an unpleasant feeling (VAS = 2). The pain was described by all patients as

A. BORGEAT, MD, D. KWIATKOWSKI, MD, Department of Orthopaedics, University of Zurich/Balgrist, Switzerland.
Accepted for publication: April 10, 1997.
Address for correspondence: Department of Orthopaedics, University of Zurich/Balgrist, Forchstrasse 340, CH-8008 Zurich, Switzerland.

intense and burning. The first eight patients had sudden flexion of the elbow and wrist at the same time; the two others showed only slight flexion of the wrist.

In the second part of the study all five patients complained of severe burning pain after the first injection with flexion of the elbow and wrist, as described previously (VAS = 10). In contrast, after the second injection three patients had moderate pain (VAS = 4) and the other two only an unpleasant feeling (VAS = 2). All five patients reported that pain was greatly decreased during the second injection. No erythema or any change in the skin surrounding the point of injection or the arm was observed. Twenty-four hours later there was no vein induration and no patient complained of residual pain. At the end of the surgical procedure, patients recalled the pain, but none had any memory of respiratory difficulties.

In the third part of the study no patient complained of pain (VAS = 0) when receiving either 0.9% NaCl pH 5.3 or 0.9% NaCl adjusted at pH 4.

Comment

We have demonstrated that administration of rocuronium was associated with severe burning pain on injection which lasted for approximately 10–20 s. In most cases brisk flexion of the elbow and wrist was observed simultaneously during i.v. injection of rocuronium. Interestingly, after a short interval of time, the pain was greatly decreased during a subsequent second administration of the drug.

Our results confirm earlier reports[3–5] describing the burning pain associated with administration of rocuronium before induction of anaesthesia. Of interest is the observation that the brisk flexion of the elbow and wrist noted in patients after induction of anaesthesia was similar in nature and duration to that observed in awake patients.

The mechanism by which rocuronium causes pain is unclear. Rocuronium is supplied in a sterile, non-pyrogenic, isotonic solution. Isotonicity is obtained with sodium chloride and a pH of 4 by adding acetic acid or sodium hydroxide. The osmolality (osmol $litre^{-1}$) and osmolarity (osmol kg^{-1}) are between 260 and 330.[6] The relatively low pH of the rocuronium solution may be a possible cause, as Klement and Arndt[7] have shown that injection of acidic solutions with a pH of 4 or less causes pain on injection, which increased linearly with a lower pH. However, the authors noted that after injection of acidic solutions, perivenous oedema developed immediately and was followed by thrombophlebitis for up to 3 weeks, which was not the case in this study.[7] Moreover, the absence of pain in patients receiving 0.9% NaCl 1 ml adjusted to pH 4 argues against such a possibility. Interestingly, vecuronium is buffered at a pH of 4 and has not been associated with pain on injection.

The short duration of the pain and marked decrease or absence of pain during a subsequent second administration led us to speculate that local release of mediators may be implicated in this reaction. Histamine is unlikely as neither erythema nor warmth in the surrounding tissue was observed or reported. Other mediators such as a kininogen cascade may be involved; this was postulated to explain the pain associated with propofol injection.[8] The pain associated with propofol and rocuronium is similar: it appears immediately during administration, duration is short and intensity decreases with subsequent injection.

Rocuronium should not be given to awake patients (e.g. priming). We believe that the similarities of movements of the arm observed in the awake patient and after induction of anaesthesia indicate that the movements observed in anaesthetized patients are the direct consequence of pain associated with administration of rocuronium. In order to avoid this side effect, it is important to inject rocuronium only when a deep stage of unconsciousness has been reached.

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